REMARKS

Reconsideration is requested.

Claims 35, 36 and 43-67 are pending.

Claims 50, 55 and 56 have been canceled, without prejudice, above. Upon entry of the present Amendment, claims 35, 36, 43-49, 51-54 and 57-67 will be pending.

Entry of the present Amendment is requested.

Revised claim 35 specifies that the recited vector is a plasmid or a recombinant viral vector. Claims 43-46, 54 and 64-67 are believed to have been revised in a manner suggested by the Examiner. Specifically, the reference to functional fragments and portions objected to by the Examiner have been removed by the above amendments. Moreover, the phrase "suitable for" has been deleted from claim 54. support for the revisions to claim 54 may be found, for example, in unamended claims 43-46 and page 3, lines 35, of the specification.

The present amendments are made without prejudice or disclaimer and solely in order to facilitate reconsideration of this application. In particular, applicant reserves his right to file a continuation and/or divisional application(s) at a later stage, and the present amendment shall not be considered as an admission of the objection or as a waiver of any subject matter.

The Section 112, first paragraph "written description", rejection of claims 43-46 and 64-67 is believed to be obviated by the above amendments. Entry of the present Amendment will at least reduce the issues for appeal by obviating this rejection. Entry of the Amendment and withdrawal of the rejection are requested.

To the extent not obviated by the above amendments, the Section 112, first paragraph "enablement", rejection of claims 35, 43-46, 54-56 and 64-67 is traversed. Reconsideration and withdrawal of the rejection are re quested in view of the above and the following comments.

Claim 35 to include the details of claim 50, which was not rejected for an alleged lack of enabling support.

Claims 55 and 56 referring to compositions for treating a human disease have been deleted according to the Examiner's suggestions and claim 54 has been amended.

Claim 54 specifies that the vector is for in vitro or ex vivo transgene delivery and is believed to precisely identify the post transcriptional regulatory elements, as explained previously.

The Examiner is urged to appreciate however that the specification provides enabling and written description support for the broad family of vectors (see for example, page 11, lines 1-14). The authors of the attached Brun *et al.* ("Optimization of Transgene Expression at the Posttranscriptional Level in Neural Cells: Implications for Gene Therapy", Molecular Therapy, Vol. 7, No. 6, 782-789, June 2003) is submitted as evidence confirming the efficiency of a vector according to the invention, using two different kinds of vectors from the above mentioned family, i.e., plasmids and recombinant viruses. Specifying the nature of the vector should not be required for one of ordinary skill in the art to make and use the claimed invention without reasonable experimentation.

The present application will be understood to teach the use of a chimeric genetic construct comprising a transgene operably linked to at least two distinct postranscriptional regulatory elements functional in mammalian cells, each comprising a UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR to increase transgene expression at the posttranscriptional level.

The Examiner's comments relating to methods comprising expressing a transgene encoded by vectors in fibroblasts and neuronal cells *in vivo* are believed to be obviated by the above amendments..

Entry of the present Amendment and consideration of the attached will at least reduce the issues for appeal by obviating this rejection. Entry of the Amendment and withdrawal of the rejection are requested.

The Section 103 rejections of claims 35, 36 and 46 over Barry (Human Gene Therapy 12:1103-1108; 2001) in view of Paulding (JBC 274:2532-2538); of claim 43 over Barry, Paulding and Ramezani (Molecular Therapy 2:458-469; 2000); of claims 40, 44 and 64-65 over Barry, Paulding, Ramezani and Rogers (JBC 274:6421-6431; 1999); of claims 41-42, 45-51 and 66-67 over Barry, Paulding, Ramezani, Rogers and Aronov (J. Mol. Nerurosci., 12:131-145; 1999); and of claims 52, 56 and 59 over Barry and Chang (Curr. Gene Ther. 2:237-251; 2001), are traversed..

Reconsideration and withdrawal of the rejections are requested as the applicants believe that the cited art, and in particular the cited Barry et al., fail to describe or suggest a vector wherein each of the two distinct posttranscriptional regulatory

elements comprises a UTR region of a eukaryotic mRNA selected from a WPRE element, tau 3'UTR, TH3'UTR and APP5'UTR. The Barry et al. reference further does not suggest that synergistic effects could be obtained by combining at least two distinct posttranscriptional regulatory elements.

The applicants have tested combinations of these posttranscriptional regulatory elements and unexpectedly found that they could cooperate or act in synergy to provide positive effects on transgene expression. This is confirm by the enclosed declaration form Dr Jacques Mallet, inventor, and by the attached Brun *et al.* reference. Consideration of the attached and withdrawal of the Section 103 rejections are requested. The applicants submit that the cited combination of art would not have suggested the vector according to the claimed invention not its effect in enhancing expression of the transgene.

Withdrawal of the Section 103 rejections is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

Respectfully submitted,

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